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FOLEY AND LARDNER LLP			SASAN, ARADHANA	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/550,453	Applicant(s) FISCHER ET AL.	
	Examiner ARADHANA SASAN	Art Unit 1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 July 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 64-81 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 64-81 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 26 September 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>09/26/05 & 07/16/09</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Restriction Response

1. Applicant's election of Group II (claims 64-68 and new claims 69-81), drawn to a method for treating a patient suffering from pain, in the reply filed on July 16, 2009 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). The restriction requirement is therefore made FINAL.
2. Claims 1-63 were canceled.
3. Claims 64-81 are included in the prosecution.

Priority

4. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Information Disclosure Statement

5. The information disclosure statements (IDS) submitted on 09/26/05 and 07/16/09 are acknowledged. Documents A34 (DE 2332484) and A35 (DE 2415490) from the IDS filed on 07/16/09 were not in English and were not considered.
See attached copies of Form PTO-1449.

Specification

6. The use of the trademarks DOCONTIN®, MS CONTIN®, KADIAN™, and MST CONTINUS® has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

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Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Objections

7. Claim 77 is objected to because of the following informalities: The claim is missing a period at the end of the sentence. Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 64-77 and 79-81 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically all the claims above recite “an opioid”, this type of claim is considered a **reach through** claim. The claims are considered reach through claims because as amended the claims would read upon opioids yet to be invented, thus the limitations of the opioid are reach through claims. To expedite the examining process the examiner simply searched for the opioids claimed in latter dependent claim (claim 78 has morphine sulfate).

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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11. Claims 64, 67, and 78 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 64 recites: "A method for treating a patient suffering from pain sensitive to an opioid comprising orally administering such opioid ...". It is unclear if the patient is sensitive to an opioid. It is recommended that the term "and" or the term "that is" be added between the terms "pain" and "sensitive". It is also recommended that a comma be added before the term "comprising".

13. Claim 64, line 8 recites "... a coating that is substantially insoluble in ...". The term "substantially insoluble" is not defined in the specification and it is unclear what is encompassed by "substantially insoluble".

14. Claim 64, line 9 recites the phrase "...intended release period...". This phrase is not defined in the specification and it is unclear how long or what period of time is encompassed by "intended release period".

15. Claim 67 recites "less side effects". It is unclear what is considered "less side effects", if there is a minimum requirement for "less side effects" or if there is a measurable or quantifiable scale for the "side effects".

16. Claims 78, line 2 recites "... an equivalently effective opioid". The specification does not define "an equivalently effective opioid" and it is unclear which opioids are included or excluded from being "equivalently effective".

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

18. Claims 64-65 and 79-81 are rejected under 35 U.S.C. 102(b) as being anticipated by Bar-Shalom et al. (US 5,213,808).

The claimed invention is a method for treating a patient suffering from pain sensitive to an opioid, comprising orally administering such opioid in a controlled release pharmaceutical composition comprising a matrix composition comprising: a) a polymer or a mixture of polymers, b) an opioid, and optionally, c) one or more pharmaceutically acceptable excipients, the matrix composition being provided with a coating that is substantially insoluble in and impermeable to fluids during the intended release period, the coating comprising one or more polymers selected from the group consisting of ethylcellulose, cellulose acetate, polyamide, polyethylene, polyethylene terephthalate, polypropylene, polyurethane, polyvinyl acetate, polyvinyl chloride, silicone rubber, latex, polyhydroxybutyrate, polyhydroxyvalerate, teflon, polylactic acid or polyglycolic acid and copolymers thereof, ethylene vinyl acetate (EVA), styrene-butadienestyrene (SBS) and styrene- isoprene-styrene (SIS), the coating having at least

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one opening exposing at least one surface of the matrix, thereby allowing controlled release of the opioid by erosion of the matrix surface.

Bar-Shalom teaches treatment of rheumatoid arthritis or related disorders by administering an article for controlled delivery of an active substance (Abstract). The composition comprises at least one active substance, a matrix comprising polymers, and a coating having at least one opening exposing at least one of the inner layers (Col. 3, lines 21-66). A constant release of the active substance over a period of time that does not require administration of the drug several times a day is disclosed (Col. 5, lines 3-11). Morphine is disclosed as an active substance (Col. 9, line 7). Polyethylene glycols are disclosed as the fillers used in combination with the active substance (Col. 10, lines 14-16 and 27). Examples of coating materials which disintegrate or crumble after erosion of the transverse layers of the composition are cellulose acetate, polyamide, polyethylene, polyethylene terephthalate, polypropylene, polyurethane, polyvinyl acetate, polyvinyl chloride, silicone rubber, latex, polyhydroxybutyrate, polyhydroxyvalerate, teflon, polylactic acid or polyglycolic acid and copolymers thereof, copolymers such as ethylene vinyl acetate (EVA), styrene-butadiene-styrene (SBS) and styrene-isoprene-styrene (SIS) (Col. 16, lines 26-36).

Therefore, the limitations of claims 64-65 and 79-81 are anticipated by the teachings of Bar-Shalom.

19. Claims 64-68 and 76-81 are rejected under 35 U.S.C. 102(e) as being anticipated by Fischer et al. (US 2004/0253310 A1).

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art

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under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Fischer teaches a method for treating a patient suffering from pain comprising administering an opioid in a controlled release composition, the composition comprises a matrix comprising an opioid, a polymer or a mixture of polymers, optionally one or more pharmaceutically acceptable excipients and a coating with at least one opening (Page 17, claim 1, Page 19, claims 54-58). "The active substance is released into an aqueous medium by erosion of at least one surface of the composition ... the ... active substance is typically an opioid such as morphine or a glucuronide thereof. The coating comprises a first cellulose derivative which is substantially insoluble in the aqueous medium and at least one of a) a second cellulose derivative which is soluble or dispersible in water, b) a plasticizer, and, d) a filler" (Abstract). Figure 4 discloses the results of a pharmacokinetic pilot study where morphine compositions were administered to 16 volunteers (Figure 4, Pages 16-17, [0243] – [0247]). Another study was conducted in patients suffering from chronic pain (Page 17, [0248]). A composition comprising morphine sulfate and polyethylene oxide 200,000 was prepared and dissolution studies show release of morphine sulfate from 1 to 8 hours (Page 15, Example 1, [0231] – [0234]). The use of polyglycols as suitable polymers in the composition is disclosed (Page 5, [0076]). The composition can be administered 1-2 times or 1 times daily (Page 12, [0166]). Measuring the degree of pain treatment by using a 4-point verbal rating scale is disclosed (Page 19, claim 56).

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Therefore, all the limitations of claims 64-68 and 76-81 are anticipated by the teachings of Fischer.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

21. Claims 69-75 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fischer et al. (US 2004/0253310 A1).

The teaching of Fischer is stated above.

Fischer does not expressly teach the mean plasma concentration after various time periods that is a percentage of the mean maximal concentration obtained by the dose.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of treating pain by administering a composition comprising morphine sulfate in a matrix comprising polymers and a coating having at least one opening, as suggested by Fischer, determine the mean plasma concentration over different time periods during the process of routine experimentation, and produce the instant invention.

One of ordinary skill in the art would do this because Fischer teaches the determination of plasma concentration (Figure 4). One of ordinary skill in the art would

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find it obvious to determine the mean maximal concentration obtained by a particular dose and the percent of that dose for a particular time point.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

The limitations of claims 69-75 related to the mean plasma concentration after specific time periods are rendered obvious by the results of the study shown in Figure 4 (plasma concentration of morphine sulfate over 24 hours) by Fischer.

22. Claims 66-78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bar-Shalom et al. (US 5,213,808) in view of Fischer et al. (US 2004/0253310 A1) .

The teaching of Bar-Shalom is stated above.

Bar-Shalom does not expressly teach the measurement of the degree of pain or the mean plasma concentration obtained by the dose.

The teaching of Fischer with respect to measuring the degree of pain treatment by using a 4-point verbal rating scale is stated above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of treating pain (patients with rheumatoid arthritis) by administering a composition comprising an active substance, a matrix comprising polymers, and a coating having at least one opening exposing at least one

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of the inner layers, as suggested by Bar-Shalom, use different rating scales to measure the degree of pain and determine the mean plasma concentration over different periods, as suggested by Fischer, and produce the instant invention.

One of ordinary skill in the art would do this because in order to determine the efficacy of the pain treatment method, one would employ various pain rating scales, depending on patient compliance and ease of computing the results.

Regarding instant claim 66, the limitation of measuring the degree of pain would have been obvious over the treatment of rheumatoid arthritis taught by Bar-Shalom (Abstract) in view of measuring the degree of pain treatment by using a 4-point verbal rating scale, as taught by Fischer (Page 19, claim 56). In order to determine the efficacy of the pain treatment method, one would employ various pain rating scales, depending on patient compliance and ease of computing the results. The recited verbal pain rating scale would have been an obvious variant unless there is evidence of criticality or unexpected results.

Regarding instant claims 67 and 68, the limitation of less side effects of the treatment when compared to a treatment with a similar amount of opioid in an immediate release composition would have been obvious over the less side effects of the treatment when compared to a treatment with a similar amount of opioid in an immediate release composition, as taught by Fischer (Page 19, claims 57 and 58).

Regarding instant claims 69-75, the limitation of the mean plasma concentration over different periods would have been obvious over the plasma concentration of morphine, as taught by Fischer (Figures 4 and 5 and Page 17, [0244] – [0248]).

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Regarding instant claims 76-77, the limitation of once or twice daily administration of the composition would have been obvious over the composition that can be administered 1-2 times or 1 times daily, as taught by Fischer (Page 12, [0166]).

Regarding instant claim 78, the limitation of 15-300mg of morphine sulphate would have been obvious over the composition comprising 30mg of morphine sulphate, as taught by Fischer (Page 15, [0235]).

Double Patenting

23. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

24. Claims 64-81 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3-47, and 49-71 of copending Application No. 10/550,685 (the ‘685 Application).

Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims and claims of the ‘685 Application are drawn to

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coated matrix composition. The difference between instant claims and those of the '685 Application is that instant claims are drawn to a method of treating a patient suffering from pain. However, instant claims were amended to include the limitations of a coated matrix composition for administration. Thus, the limitations of the coated matrix composition are obvious over claims of the '685 Application, and thus they are not patentably distinct over each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

25. Claims 64-81 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 60-100 of copending Application No. 12/078,312 (the '312 Application).

Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims and claims of the '312 Application are drawn to coated matrix composition and a method of treating a patient suffering from pain. The difference is that claims of the '312 Application require specific excipients in the matrix composition. However, one of ordinary skill in the art would find it obvious to use various pharmaceutically acceptable excipients in the matrix composition based on the compatibility of the excipient with the chosen active ingredient and the recited excipients of the '312 Application would be obvious variants. Thus, the claims directed to a method of treatment of a patient suffering from pain by administering a coated matrix composition are obvious over claims of the '312 Application, and thus they are not patentably distinct over each other.

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This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert A. Wax, can be reached at 571-272-0623. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Aradhana Sasan/
Examiner, Art Unit 1615

/Robert A. Wax/
Supervisory Patent Examiner, Art Unit 1615